

| L Number | Hits | Search Text | DB | Time stamp |
|----------|-------|---|---|------------------|
| - | 12 | ((kingsman NEAR (susan or alan) NEAR (mary OR alan)) and retrovir\$9) and intron | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 15:28 |
| - | 36978 | retrovir\$6 or lentivir\$9 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 15:12 |
| - | 942 | (retrovir\$6 or lentivir\$9) SAME intron | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 14:54 |
| - | 5156 | splice NEAR (donor OR acceptor) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 16:01 |
| - | 52 | ((retrovir\$6 or lentivir\$9) SAME (splice NEAR (donor OR acceptor))) SAME intron | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 14:51 |
| - | 8 | (retrovir\$6 or lentivir\$9) SAME split NEAR intron | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 14:54 |
| - | 78 | kingsman NEAR (susan or alan) NEAR (mary OR alan) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 14:55 |
| - | 52 | (kingsman NEAR (susan or alan) NEAR (mary OR alan)) and retrovir\$9 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 14:57 |
| - | 48 | ((retrovir\$6 or lentivir\$9) SAME (splice NEAR (donor OR acceptor))) SAME intron) AND REV\$9 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 15:01 |
| - | 19 | ((retrovir\$6 or lentivir\$9) SAME (splice NEAR (donor OR acceptor))) SAME intron) AND ((REV NEAR response)OR RRE) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 15:02 |
| - | 37 | (retrovir\$6 or lentivir\$9) AND (tat NEAR inducible) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 15:14 |
| - | 10 | (retrovir\$6 or lentivir\$9) SAME (tat NEAR inducible) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 15:16 |
| - | 13 | (retrovir\$6 or lentivir\$9) SAME ((tat OR REV) NEAR inducible) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 15:16 |
| - | 464 | (retrovir\$6 or lentivir\$9) SAME (splice NEAR (donor OR acceptor)) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 15:24 |
| - | 16 | ((retrovir\$6 or lentivir\$9) SAME (splice NEAR (donor OR acceptor))) and intron.clm. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 15:24 |
| - | 2 | WO NEAR "9817817" | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 15:28 |
| - | 12 | (US-6312683-\$ or US-6242187-\$ or US-6228639-\$ or US-6143520-\$).did. or (US-20030147907-\$ or US-20040013648-\$ or US-20020141978-\$).did. or (WO-9817817-\$ or WO-2083728-\$ or EP-1164196-\$ or GB-2331522-\$).did. or (EP-931157-\$).did. | USPAT; US-PGPUB; EPO; DERWENT | 2004/04/09 15:29 |

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|---|-------|---|---|------------------|
| - | 12 | (US-6312683-\$ or US-6242187-\$ or US-6228639-\$ or US-6143520-\$).did. or (US-20040013648-\$ or US-20020141978-\$ or US-20030147907-\$).did. or (WO-2083728-\$ or EP-1164196-\$ or WO-9817817-\$ or GB-2331522-\$).did. or (EP-931157-\$).did. | USPAT; US-PGPUB; EPO; DERWENT | 2004/04/09 15:30 |
| - | 24514 | 435/320.1.ccls. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 16:00 |
| - | 11768 | 435/320.1.ccls. and (retrovir\$6 OR lentivir\$6) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 16:01 |
| - | 1838 | (435/320.1.ccls. and (retrovir\$6 OR lentivir\$6)) and (splice NEAR (donor OR acceptor)) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 16:02 |
| - | 67 | ((435/320.1.ccls. and (retrovir\$6 OR lentivir\$6)) and (splice NEAR (donor OR acceptor))) and intron.clm. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 16:08 |
| - | 301 | 435/320.1.ccls. and (TIN OR TRIN) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2004/04/09 16:09 |

| L Number | Hits | Search Text | DB | Time stamp |
|----------|-------|--|---|------------------|
| - | 37 | KINGSMAN-ALAN-JOHN and retrovir\$15 | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2004/04/09 15:20 |
| - | 1 | LISZIEWCZ-JULIANNA | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:51 |
| - | 3 | WO ADJ "9614332" | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:51 |
| - | 50 | KINGSMAN-ALAN-JOHN | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2004/04/09 14:25 |
| - | 33712 | retrovir\$15 | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:56 |
| - | 102 | retrovir\$15 and (HIV WITH U3 WITH R) | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:56 |
| - | 33712 | retrovir\$15 | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:56 |
| - | 22958 | (435/320.1).CCLS. | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:57 |
| - | 3393 | ((435/320.1).CCLS.) and (((retrovir\$15 and (MULV or MLV or moMLV or murine or moloney)) and (U3 or rre or rev or tat or LTR)) and (donor or acceptor)) and HIV) | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:57 |
| - | 758 | vector SAME (TRIN or TIN) | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:57 |
| - | 164 | retrovir\$15 and (HIV WITH U3) | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:57 |
| - | 2 | LISZIEWCZ-J\$15 | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:57 |
| - | 2 | wo ADJ "9915683" | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/12/08 14:57 |

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|---|----|--|---|------------------|
| - | 3 | ((US-6312682-\$ or US-6235522-\$ or US-6132731-\$ or US-6168916-\$ or US-6096538-\$ or US-6218187-\$ or US-6207455-\$ or US-6165782-\$ or US-6051427-\$ or US-5994136-\$ or US-5981276-\$ or US-5858740-\$ or US-5834256-\$ or US-5693508-\$ or US-5665577-\$ or US-5380830-\$ or US-6025124-\$).did. or (GB-2331522-\$ or WO-9817817-\$ or WO-9817815-\$ or WO-9817816-\$ or WO-9727310-\$ or WO-9631602-\$ or WO-9637623-\$ or WO-9614332-\$ or WO-9915683-\$).did. or (US-5693508-\$ or EP-827545-\$).did.) and (retrovir\$15 and (MULV or MLV or moMLV or murine or moloney)) and (U3 or rre or rev or tat or LTR or splice)) and donor.clm. | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2004/04/09 14:20 |
| - | 11 | Retrovir\$5 and TRIN | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:57 |
| - | 25 | (vector SAME (TRIN or TIN)) and retrovir\$5 | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:57 |
| - | 59 | (retrovir\$15 and (HIV WITH U3 WITH R)) and REV | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2003/12/08 14:57 |
| - | 31 | (US-6218187-\$ or US-6207455-\$ or US-6165782-\$ or US-5994136-\$ or US-6051427-\$ or US-5981276-\$ or US-5858740-\$ or US-5834256-\$ or US-5693508-\$ or US-5665577-\$ or US-5380830-\$ or US-6312682-\$ or US-6235522-\$ or US-6168916-\$ or US-6132731-\$ or US-6096538-\$ or US-6025124-\$).did. or (US-20020141978-\$).did. or (WO-9614332-\$ or WO-9915683-\$ or GB-2331522-\$ or WO-9817817-\$ or WO-9817816-\$ or WO-9817815-\$ or WO-9727310-\$ or WO-9637623-\$ or WO-9631602-\$ or EP-1164196-\$ or GB-2344592-\$).did. or (EP-827545-\$ or US-5693508-\$).did. | USPAT; US-PGPUB; EPO; DERWENT | 2003/12/08 14:59 |
| - | 40 | KINGSMAN-ALAN-JOHN and retrovir\$15 | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2004/04/09 14:17 |
| - | 54 | KINGSMAN WITH ALAN WITH JOHN | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2004/04/09 14:26 |
| - | 46 | KINGSMAN WITH susan WITH mary | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2004/04/09 14:26 |
| - | 66 | (KINGSMAN WITH ALAN WITH JOHN) or (KINGSMAN WITH susan WITH mary) | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2004/04/09 14:27 |

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|---|-----|--|---|------------------|
| - | 44 | ((KINGSMAN WITH ALAN WITH JOHN) or (KINGSMAN WITH susan WITH mary)) and retrovir\$6 | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2004/04/09 14:30 |
| - | 367 | Naldini NEAR Luigi OR Trono NEAR didier OR verma NEAR inder OR Baltimore NEAR David OR Sodroski NEAR Joseph OR LISZIEWCZ NEAR JULIANNA OR Haseltine NEAR William | USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR | 2004/04/09 15:21 |

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(FILE 'HOME' ENTERED AT 15:35:21 ON 09 APR 2004)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
AT 15:36:11 ON 09 APR 2004

L1 114693 S RETROVIR? OR LENTIVIR?
L2 1311 S L1 AND ((SPLICE DONOR) OR (SPLICE ACCEPTOR) OR SA OR SD)
L3 108 S L2 AND INTRON
L4 52 DUP REM L3 (56 DUPLICATES REMOVED)
L5 26 S L4 AND PY<=1996
L6 26 FOCUS L5 1-
L7 39 S L1 AND (TRIN OR TIN)
L8 25 DUP REM L7 (14 DUPLICATES REMOVED)
L9 25 SORT L8 PY
E KINGSMAN SUSAN?/AU
L10 34 S E2
L11 102 S E1
E KINGSMAN ALAN?/AU
L12 32 S E1
L13 148 S L10 OR L11 OR L12
L14 141 DUP REM L13 (7 DUPLICATES REMOVED)
L15 64 S L1 AND L14
L16 3 S L2 AND L14

=> d an ti so au ab pi l16 1-3

L16 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:781146 CAPLUS

DN 135:340191

TI HIV-1 and EIAV derived **retroviral** vector constructs with
codon-optimized gag-pol genes and their uses

SO PCT Int. Appl., 201 pp.

CODEN: PIXXD2

IN **Kingsman, Alan John**; Kim, Narry; Kotsopoulou, Ekaterini; Rohll,
Jonathan; Mitrophanous, Kyriacos Andreou

AB This invention claims a method of producing a replication defective
retrovirus comprising transfecting a producer cell with the
following: (i) a **retroviral** genome; (ii) a nucleotide sequence
coding for **retroviral** gag and pol proteins; and (iii) nucleotide
sequences encoding other essential viral packaging components not encoded
by the nucleotide sequence of (ii); characterized in that the nucleotide
sequence coding for **retroviral** gag and pol proteins is codon
optimized for expression in the producer cell. The invention provides
synthetic gag-pol polynucleotide sequences which will not be able to
recombine or package viral mRNAs in infected cells. Codons in the region
of the gag-pol gene which contains overlapping reading frames encoding gag
and pol proteins are not optimized, to ensure efficient expression of the
gag and pol proteins. The codon-optimized gag-pol sequences for HIV-1 and
EIAV (equine infectious anemia virus) disrupt packaging signals near the
5' end of the gag-pol mRNA and also result in Rev/RRE-independent gag-pol
mRNA expression and protein production. An example of the invention is an
HIV-1 based vector system composed of three plasmids: one expressing
codon-optimized gene gag-pol; one expressing VSV-G envelope proteins; and
one expressing a 360-nucleotide "wild-type" gag sequence and a
splice donor. RNA expression, protein expression,
titers, and transduction efficiency of the system were determined. A similar
vector system based on the non-primate **lentivirus** EIAV was
constructed and characterized; however, sequences in the gag gene required
for packaging EIAV appear to differ from the HIV-1 packaging signal.

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2001079518 A2 20011025 WO 2001-GB1784 20010418
WO 2001079518 A3 20020516

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,

RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 EP 1278878 A2 20030129 EP 2001-921651 20010418
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2004508808 T2 20040325 JP 2001-577501 20010418

L16 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:119767 CAPLUS

DN 132:304043

TI Split-intron **retroviral** vectors: enhanced expression with improved safety

SO Journal of Virology (2000), 74(5), 2365-2371

CODEN: JOVIAM; ISSN: 0022-538X

AU Ismail, Said I.; **Kingsman, Susan M.**; Kingsman, Alan J.; Uden, Mark

AB The inclusion of **retrovirus**-derived introns within **retrovirus**-based expression vectors leads to a fraction of the resulting transcripts being spliced. Such splicing has been shown to markedly improve expression. One way to improve upon this still further might involve the use of more efficient introns instead of those from the provirus. Currently, however, incorporation of such introns remains self-defeating since they are removed in the nucleus of the producer cell. In the past, elaborate ways to overcome this problem have included the use of alphaviruses to make the vector transcripts within the cytoplasm, thus avoiding the nuclear splicing machinery during vector production. The authors now present a novel design for the inclusion of introns within a **retroviral** vector. In essence, this is achieved by exploiting the **retroviral** replication process to copy not only the U3 promoter but also a synthetic **splice donor** to the 5'-long-terminal-repeat position during reverse transcription. Once copied, synthesized transcripts then contain a **splice donor** at their 5' end capable of interacting with a consensus **splice acceptor** engineered downstream of the packaging signal. Upon transduction, the authors demonstrate these vectors to produce enhanced expression from near fully spliced (and thus packaging signal minus) transcripts. The unique design of these high titer and high-expression **retroviral** vectors may be of use in a number of gene therapy applications.

L16 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:268635 CAPLUS

DN 128:291139

TI Construction of TRIN **retroviral** vectors containing Rev-responsive element of HIV1 virus

SO PCT Int. Appl., 38 pp.

CODEN: PIXXD2

IN **Kingsman, Susan Mary**; **Kingsman, Alan John**

AB **Retroviral** vector particles having an RNA genome carrying sequences which provide in the DNA provirus at least one selected gene located within an intron in a transcription unit of the provirus, which transcription unit further comprises a polynucleotide response element which is responsive to a nucleus to cytoplasm transport factor such as HIV Rev. These vectors have been named TRIN (Tat and Rev inducible) vectors. Expression of the selected genes is thus rendered Rev-dependent and so is dependent upon the presence of HIV. The TRIN vectors also contain the murine leukemia virus **splice donor** site, the strong CMV promoter, a packaging signal, and the HIV U5 and R regions.

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
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|----|------------|----|----------|----------------|----------|
| PI | WO 9817817 | A1 | 19980430 | WO 1997-GB2859 | 19971017 |
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W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
 GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
 GN, ML, MR, NE, SN, TD, TG

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|--|----|----------|----------------|----------|
| AU 9747124 | A1 | 19980515 | AU 1997-47124 | 19971017 |
| GB 2331989 | A1 | 19990609 | GB 1999-4143 | 19971017 |
| GB 2331989 | B2 | 20000927 | | |
| EP 931157 | A1 | 19990728 | EP 1997-909438 | 19971017 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2001502904 | T2 | 20010306 | JP 1998-519088 | 19971017 |
| US 2002141978 | A1 | 20021003 | US 1999-254529 | 19990804 |

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